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Original article

Incidence and clinical impact of fracture of drug-eluting stents widely used in current clinical practice: Comparison with initial platform of sirolimus-eluting stent

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ABSTRACT

Background: Almost all data on drug-eluting stents (DES) fracture have been derived from initial platform of first-generation DES such as Cypher Bx® (CBX) and Taxus Express®. However, incidence and clinical impact of fracture of newer DES platforms (including Cypher Select®, Taxus® Liberté™, Endeavor®, and Xience™ V) that have been used widely in current clinical practice have not yet been studied.
Methods and results: We analyzed data of 1518 lesions treated with the newer DES platforms in patients who underwent follow-up coronary angiography and compared the results with those of 622 lesions treated with the CBX. The group of newer DES platforms showed significantly lower incidence of stent fracture (SF) than the CBX group (1.25% vs. 5.8%, $p < 0.001$). Binary restenosis (42.1% vs. 6.6%, $p < 0.001$) and target lesion revascularization (TLR) (47.3% vs. 6.2%, $p < 0.001$) related to SF in the newer DES platforms' group were significantly higher than those not related to SF. Notably, SF-related binary restenosis (42.1% vs. 36.1%, $p = 0.52$) and TLR (47.3% vs. 41.6%, $p = 0.2$) were similar between the newer DES platforms' group and the CBX group. On multivariable logistic regression analysis, lesion angulation >45° (odds ratio [OR]: 7.6; 95% confidence interval [CI]: 2.2–26.31), RCA stenting (OR: 5.14; 95% CI: 1.62–16.3) and total stent length (OR: 1.18; 95% CI: 1.03–1.33) were identified as independent predictors for fracture of the newer DES platforms, while closed-cell design stent (Cypher Select®) was not.
Conclusions: Although implantation of the newer DES platforms might reduce the occurrence of SF compared with the CBX, SF-related binary restenosis and TLR remain similarly high. And to predict SF in the newer DES platforms' era, lesion characteristics on index procedure are more important than implanted stent design.

Introduction

Although stent fracture (SF) is an uncommon complication of drug-eluting stents (DES), its occurrence may be associated with clinically serious complications such as restenosis, stent thrombosis, and aneurysm formation. Several studies have reported on the incidence, predictors, and clinical impact of DES fracture [1–3]. However, when we reviewed previous reports, almost all data on DES fracture were derived from the initial platform of first-generation DES, mainly from the initial platform of sirolimus-eluting stent [i.e. Cypher Bx® (CBX), Cordis, Johnson and Johnson Corp., Miami, FL, USA] and paclitaxel-eluting stent (i.e. Taxus Express®, Boston Scientific Corp., Natick, MA, USA) [1–3].

In current clinical practice, the majority of physicians have performed percutaneous coronary intervention (PCI) using newer DES platforms, such as Cypher Select® (CS) (Cordis, Johnson and Johnson Corp.)/Taxus® Liberté™ (TL) (Boston Scientific Corp.)/Endeavor®

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(EN) (Medtronic Cardiovascular, Minneapolis, MN, USA)/Xience^{TM} V (XV) (Abbott Vascular, Abbott Park, IL, USA) rather than the initial platforms of first-generation DES. Although the newer DES platforms have been upgraded in terms of both mechanical and material properties, clinical information on SF remains to be determined. This is in contrast to the well-known dataset of initial platforms of first-generation DES. We identified the incidence, predictors, and clinical impact of fracture in newer DES platforms including CS, TL, EN, and XV, and compared results with those of initial platform of first-generation CBX as a control group.

Methods

Study population and procedure

We retrospectively analyzed data from the Catholic Medical Center Percutaneous Coronary Intervention (COACT) registry, which is a multicenter, observational, all-comers registry of 9292 patients who underwent PCI with DES at 8 participating hospitals from September 2003 to December 2009. This study complied with the Declaration of Helsinki regarding investigation in humans and was approved by the institutional ethics committees at the participating hospitals. Written informed consent was obtained from each patient before enrollment. There was no industry involvement in the design, conduct, or analysis of the study. Of 1048 PCI patients with CBX, we analyzed available data for 622 consecutive lesions in 518 patients who underwent follow-up coronary angiography (CAG). We also identified a total of 4664 stented lesions treated with newer DES platforms in 4104 patients and of these, analyzed clinical and angiographic data of 1518 consecutive lesions in 1224 patients who underwent follow-up CAG. Follow-up CAG was performed irrespective of clinical symptoms and was routinely recommended 6–12 months after index procedure unless clinically necessary at an earlier time. The majority (94.5%) of enrolled patients underwent follow-up CAG routinely. Some patients underwent several times of follow-up CAG; in these cases, we calculated a follow-up duration from index PCI to final repeat angiography. All interventions were performed according to standard guidelines. All patients were prescribed aspirin (100–325 mg/day) indefinitely and clopidogrel (300–600 mg loading dose, 75 mg daily for at least six months). All CAG were reviewed by two experienced cardiologists blinded to clinical information. The SF was diagnosed on fluoroscopy or angiography, and intravascular ultrasound was not mandatory. To visualize stent strut effectively, we used the increased magnification, image without contrast and image with inverted color for all stented lesions. Quantitative coronary analysis (QCA) was performed using the computer-based edge-detection Coronary Angiography Analysis System (CAAS 5.7, Pie Medical, Maastricht, The Netherlands). SF was classified as either complete fracture (complete separation of stent segments) or partial fracture (single or multiple stent SF without separation of segment) [1]. Binary restenosis was defined as a reduction of 50% or more of the luminal diameter in the stented segment (in-stent) and the margins 5 mm proximal and distal to the stent (in-segment) at follow-up. Target lesion revascularization (TLR) was defined as repeated revascularization for ischemia owing to in-stent or in-segment restenosis.

Statistical analysis

Statistical analysis was performed using SPSS 15.0 (SPSS Inc., Chicago, IL, USA). Continuous variables except follow-up duration were presented as mean (±SD) and compared using Student's *t*-test. Categorical variables were presented as frequencies or percentages and compared using chi-square test or Fisher's exact test. We compared the median follow-up duration of each group using Mood's median test. To determine the independent predictors of SF in CBX group and newer DES platforms' group respectively, multivariable logistic regression analysis was used. Independent variables were selected according to their weight on univariate testing for entry into the multivariate model (p-values < 0.1 in Table 2) and well-known established predictors (closed-cell design: Cypher Select® in the newer DES platforms' group, right coronary artery [RCA] stenting in CBX group) were also entered into the analysis. We calculated odds ratio (OR) of CBX-to-newer DES platforms for SF using multivariable logistic regression analysis, for which, we merged data from both groups and introduced into the model variables that showed significant difference between patients with SF and without SF (age, RCA stenting, total stent length, stent type [CBX vs. newer DES platforms], lesion angulation >45°) (data not shown). A p-value of <0.05 was considered to indicate a significant difference.

Results

Clinical and angiographic characteristics of stent fracture

Baseline clinical and angiographic characteristics between the newer DES platforms' group and the CBX group are listed in Table 1. Patients in newer DES platforms' group had a younger age, longer lesion length, longer total stent length, and lower rates of binary restenois and TLR compared to CBX group. We also compared baseline characteristics between SF subgroup and non-SF subgroup (Table 2). In the newer DES platforms' group, patients with SF showed a higher incidence of previous myocardial infarction (MI) and coronary artery bypass graft history compared to patients in whom SF did not occur. SF mainly occurred in the RCA and the left anterior descending artery (LAD); however, no SFs were observed in the left circumflex artery (LCX). Compared with the non-SF subgroup, lesions in the SF subgroup showed more B2/C type, smaller reference diameter, longer lesion length, higher incidence of lesion angulation >45°, longer total stent length, more number of stents per lesion, and higher frequency of stent overlap. In CBX group, lesions in the SF subgroup showed more B2/C type, longer lesion length, higher incidence of lesion angulation >45°, longer total stent length, more number of stents per lesion, and higher frequency of stent overlap compared with lesions in the non-SF subgroup. In addition, comparisons of baseline characteristics between SF subgroups in the newer DES platforms' group and the CBX group are listed in Table 3.

Incidence of stent fracture

The median follow-up duration from index PCI to detection of SF was similar between the newer DES platforms' group and the CBX group (12.5 months [interquartile range [IQR]: 9.2–15.5] vs. 9.5 months [IQR: 6.3–13], $p = 0.11$) (Table 3). SF was identified in 36 of 622 lesions (5.8%) and 518 patients (6.9%) in the CBX group, and 19 of 1518 lesions (1.25%) and 18 of 1224 patients (1.47%) in the newer DES platforms' group. Notably, the incidence of SF in the CBX group was significantly higher than that of the newer DES platforms' group (5.8% vs. 1.25%, $p < 0.001$) (Fig. 1). Of the 1518 lesions in the newer DES platforms' group, 635 lesions in 508 patients were implanted with CS, 411 lesions in 329 patients with TL, 110 lesions in 88 patients with EN, and 362 lesions in 299 patients with XV. Eleven SFs were identified in the CS group (1.7%), 4 in the TL group (0.97%), 0 in the EN group (0%), and 4 in the XV group (1.1%); with the incidence being similar among stent types ($p = 0.15$) (Fig. 1). Detailed individual patient data for the 19 SF cases in the newer DES platforms' group are provided in Supplementary Table 1.

Table 1
Baseline clinical and angiographic characteristics.

Clinical characteristics (*n* = no. of patients)	Newer DES platforms (*n* = 1224)	Cypher Bx (*n* = 518)	*p*
Age, years	64.4 ± 10.1	67.5 ± 7.4	0.04
Male, *n* (%)	869 (70.9)	327 (63.1)	0.12
BMI (kg/m^2)	24.3 ± 2.8	24.5 ± 2.1	0.52
Index diagnosis, *n* (%)			
Stable angina	477 (38.9)	20 (41.7)	0.58
Unstable angina	227 (18.5)	111 (21.4)	0.65
AMI	363 (29.6)	147 (28.3)	0.77
Silent ischemia	179 (14.6)	44 (8.4)	0.43
Diabetes mellitus, *n* (%)	398 (32.5)	182 (35.1)	0.58
Hypertension, *n* (%)	739 (60.3)	387 (74.7)	0.33
Current smoking, *n* (%)	386 (31.5)	140(27)	0.64
Family history of CAD, *n* (%)	150 (12.2)	66 (12.7)	0.81
Previous MI, *n* (%)	109 (8.9)	54 (10.4)	0.72
Previous CABG, *n* (%)	6 (0.4)	3 (0.5)	0.88
LVEF (%)	60.4 ± 8	58.7 ± 12	0.55
Angiographic characteristics (*n* = no. of lesions)	**Newer DES platforms (*n* = 1518)**	**Cypher Bx (*n* = 622)**	***p***
Target coronary artery, *n* (%)			
LM	34 (2.2)	4 (0.6)	0.21
LAD	715 (47.1)	212 (34)	0.45
LCX	415 (27.3)	139 (22.3)	0.74
RCA	354 (23.3)	167 (26.8)	0.66
AHA/ACC type B2/C, *n* (%)	882 (58.1)	356 (57.2)	0.87
Reference diameter (mm)	3.28 ± 0.3	3.34 ± 0.3	0.16
Lesion length (mm)	35.1 ± 15	30.1 ± 9	0.03
Diameter stenosis (%)	81 ± 15	78 ± 10	0.63
Lesion angle >45°, *n* (%)	184 (12.1)	79 (12.7)	0.77
CTO, *n* (%)	87 (5.7)	45 (7.2)	0.41
Multivessel CAD, *n* (%)	1002 (66)	398 (63.9)	0.38
Stent diameter (mm)	3.1 ± 0.27	3.12 ± 0.26	0.11
Maximum inflation pressure (atm)	14.6 ± 2.7	13.9 ± 2.5	0.58
Total stent length (mm)	37.3 ± 14.2	33.2 ± 10.3	0.02
Number of stents per lesion	1.18 ± 0.6	1.11 ± 0.4	0.65
Stent overlap, *n* (%)	288 (18.9)	70 (11.2)	0.41
Clinical outcome at follow-up, *n* (%)			
Binary restenosis	107 (7)	74 (11.9)	<0.001
TLR	102 (6.7)	55 (8.8)	0.007

Values are expressed as mean ± SD or *n* (%) of patients.
ACC, American College of Cardiology; AHA, American Heart Association; AMI, acute myocardial infarction; BMI, body mass index; CABG, coronary artery bypass graft; CAD, coronary artery disease; CAG, coronary angiography; CTO, chronic total occlusion; DES, drug-eluting stents; IQR, interquartile range; LAD, left descending artery; LCX, left circumflex artery; LM, left main coronary artery; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; RCA, right coronary artery; TLR, target lesion revascularization.

Frequencies of occurrence of partial and complete SF were similar (47.4% vs. 52.6%). While in single-stented lesions, the majority of SF were localized to the middle portion of the stent body (75%), in overlapping stents, most fractures were observed within 5-mm from areas of metal overlap (90.5%). All SFs occurred in long-stented lesions, i.e. ≥28 mm, and the longest stented lesion was 82 mm. A sizable proportion of SFs occurred at the biggest angle (hinge point) at index CAG (63%).

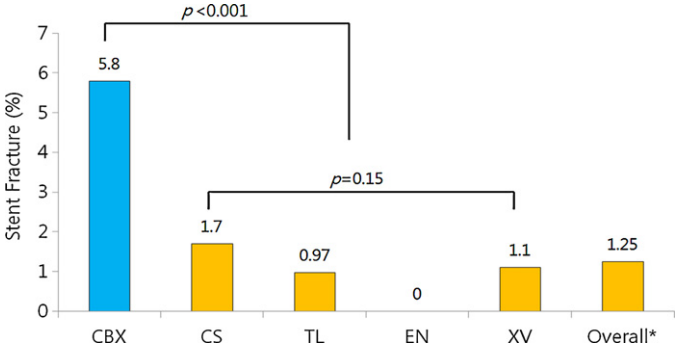

Fig. 1. Incidence of stent fracture according to stent type. Incidence of stent fracture of the CBX group (blue color) was significantly higher than that of the newer DES platforms' group (orange color). Among the newer DES platforms' group, no differences were shown in incidence of stent fracture. CBX, Cypher Bx®; CS, Cypher Select®; TL, Taxus® Liberté™; EN, Endeavor®; XV, Xience™ V; DES, drug-eluting stents. *Entire population of newer DES platforms' group. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

Clinical impact of stent fracture

In the newer DES platforms' group, a large portion of patients with SF were asymptomatic (61.1%) and some patients presented clinically with stable (33.3%) or unstable angina (10.5%) when SF was detected by angiography. Neither myocardial infarction nor stent thrombosis occurred (Table 3). While SF-related binary restenosis (42.1% vs. 6.6%, $p < 0.001$) and TLR (47.3% vs. 6.2%, $p < 0.001$) rates were significantly higher than those related with non-SF, overall incidence of binary restenosis and TLR among stent types was similar (Fig. 2). It is interesting that all binary restenosis related to SF was observed within stent (i.e. in-stent restenosis) with focal angiographic pattern. In the CBX group, a large portion of patients with SF were also asymptomatic (58.3%) at the time of SF detection (Table 3) and incidence of binary restenosis (36.1% vs. 10.4%, $p = 0.006$) and TLR (41.6% vs. 6.8%, $p < 0.001$) related with SF was significantly higher than that related with non-SF (Table 2). It is notable that SF-related binary restenosis and TLR rates of the CBX group were similar when compared with those of the CS group and

Table 2
Comparisons of baseline characteristics between fracture subgroup and non-fracture subgroup.

Clinical characteristics (*n* = no. of patients)	Newer DES platforms		*p*	Cypher Bx		*p*
	Fracture (*n* = 18)	Non-fracture (*n* = 1206)		Fracture (*n* = 36)	Non-fracture (*n* = 482)	
Age, years	63.7 ± 10.5	65.2 ± 9.3	0.72	67.9 ± 6.8	66.7 ± 9.7	0.62
Male, *n* (%)	13 (72.2)	856 (70.9)	0.98	24(67)	303(63)	0.86
BMI (kg/m^2)	24.1 ± 2.8	24.6 ± 2.8	0.46	24.3 ± 1.9	24.7 ± 2.5	0.52
Index diagnosis, *n* (%)						
Stable angina	10 (55.5)	467 (38.7)	0.35	20 (55.5)	196 (40.7)	0.43
Unstable angina	4 (22.2)	223 (18.5)	0.76	9(25)	102 (21.2)	0.64
AMI	3 (16.6)	360 (29.8)	0.24	7 (19.4)	140 (29)	0.55
Silent ischemia	2 (11.1)	177 (14.6)	0.87	0(0)	44 (9.1)	0.77
Diabetes mellitus, *n* (%)	5 (27.7)	393 (32.5)	0.67	11 (30.5)	171 (35.5)	0.6
Hypertension, *n* (%)	15 (83.3)	724 (60)	0.1	31 (86)	356 (74)	0.33
Current smoking, *n* (%)	6 (33.3)	380 (31.5)	0.85	9 (25)	131 (27.2)	0.75
Family history of CAD, *n* (%)	3 (16.6)	147 (12.1)	0.88	4 (11.1)	62 (12.8)	0.81
Previous MI, *n* (%)	5 (27.7)	104 (8.6)	0.02	4 (11.1)	50 (10.4)	0.72
Previous CABG, *n* (%)	1 (5.5)	5 (0.4)	0.006	0 (0)	3 (0.6)	0.68
LVEF (%)	61 ± 7	59 ± 10	0.43	59 ± 14	58 ± 10	0.55
Median follow-up duration months (IQR)	12.5 (9.2–15.5)	9 (6.2–13.1)	0.007	9.5 (6.3–13)	11 (8.2–15.4)	0.23

Angiographic characteristics (*n* = no. of lesions)	Newer DES platforms		*p*	Cypher Bx		*p*
	Fracture (*n* = 19)	Non-fracture (*n* = 1499)		Fracture (*n* = 36)	Non-fracture (*n* = 586)	
Target coronary artery, *n* (%)						
LM	1 (5.2)	33 (2.2)	0.64	0	4 (0.7)	0.87
LAD	8 (42)	707 (47.2)	0.82	22 (61)	290 (49.5)	0.45
LCX	0	415 (27.6)	0.03	1 (2.7)	138 (23.5)	0.21
RCA	10 (52.6)	344 (22.9)	0.05	13 (36)	154 (26.3)	0.13
AHA/ACC type B2/C, *n* (%)	19 (100)	863 (57.5)	0.001	34 (94)	322 (55)	0.001
Reference diameter (mm)	3.18 ± 0.3	3.37 ± 0.4	0.01	3.4 ± 0.3	3.28 ± 0.3	0.06
Lesion length (mm)	45.5 ± 16.2	24.7 ± 13	<0.001	36.5 ± 9.9	23.6 ± 10	<0.001
Diameter stenosis (%)	79 ± 24	85 ± 11	0.33	75 ± 10	81 ± 11	0.43
Lesion angle >45°, *n* (%)	7 (36.8)	177 (11.8)	0.007	21 (58)	58 (9.9)	0.002
CTO, *n* (%)	3 (15.8)	84 (5.6)	0.1	1 (2.7)	44 (7.5)	0.28
Multivessel CAD, *n* (%)	15 (78.9)	987 (65.8)	0.29	22 (61)	376 (64.2)	0.57
Stent diameter, mm	2.97 ± 0.32	3.2 ± 1.0	0.29	3.18 ± 0.26	3.06 ± 0.28	0.06
DES type, *n* (%)						
Cypher Select	11 (57.9)	625 (41.7)	0.58			
Taxus Liberté	4 (21)	407 (27.1)	0.68			
Endeavor	0	110 (7.3)	0.74			
Xience V	4 (21)	358 (23.9)	0.75			
Maximum inflation pressure (atm)	14.3 ± 2.6	15 ± 3.6	0.32	13.6 ± 2.5	14.2 ± 2.7	0.44
Total stent length (mm)	48.3 ± 16.8	26.3 ± 13.2	<0.001	41.2 ± 10.9	25.2 ± 10.2	<0.001
Number of stents per lesion	1.58 ± 0.6	1.18 ± 0.4	0.001	1.53 ± 0.7	1.08 ± 0.4	0.001
Stent overlap, *n* (%)	11 (57.9)	277 (18.5)	<0.001	19 (53)	51 (8.7)	<0.001
Clinical outcome at follow-up, *n* (%)						
Binary restenosis	8 (42.1)	99 (6.6)	<0.001	13 (36.1)	61 (10.4)	0.006
TLR	9 (47.3)	93 (6.2)	<0.001	15 (41.6)	40 (6.8)	<0.001

Values are expressed as mean ± SD or *n* (%) of patients except follow-up duration.
ACC, American College of Cardiology; AHA, American Heart Association; AMI, acute myocardial infarction; BMI, body mass index; CABG, coronary artery bypass graft; CAD, coronary artery disease; CTO, chronic total occlusion; DES, drug-eluting stents; IQR, interquartile range; LAD, left descending artery; LCX, left circumflex artery; LM, left main coronary artery; LVEF, left ventricular ejection fraction; MI, myocardial infarction; RCA, right coronary artery; TLR, target lesion revascularization.

entire population of the newer DES platforms' group respectively (Fig. 3).

Independent predictors of stent fracture

Fig. 4 summarizes independent predictors of SF in the newer DES platforms. On multivariable logistic regression analysis, lesion angulation >45° (OR: 7.6; 95% confidence interval [CI]: 2.2–26.3; $p = 0.001$), RCA stenting (OR: 5.14; 95% CI: 1.62–16.3; $p = 0.005$), and total stent length (OR: 1.17; 95% CI: 1.03–1.33; $p = 0.012$) were identified as statistically significant independent predictors of SF. However, stent design (closed-cell, i.e. Cypher Select®) did not hold as an independent predictor. In the CBX group, stent overlap (OR: 15.4; 95% CI: 5.67–42; $p < 0.001$), lesion angulation >45° (OR: 9.42; 95% CI: 3.7–38; $p = 0.001$), and stent diameter (OR: 7.01; 95% CI: 1.19–41.4; $p = 0.03$) were identified as independent predictors (Supplementary Fig. 1). The calculated OR of CBX-to-newer DES platforms for SF was 3.8 (95% CI: 1.86–7.8; $p < 0.001$) (data not shown).

Discussion

This is the first study to investigate incidence, clinical impact, and independent predictors of fracture in newer DES platforms which have been used widely in current clinical practice. The main findings of our study are as follows. (1) The overall SF incidence of the newer DES platforms was significantly lower than that of CBX. (2) Binary restenosis and TLR rates for lesions with SF were much higher than those for lesions without it. Notably, SF-related binary restenosis and TLR rates were not different statistically between the CBX group and the newer DES platforms' group. (3) Stenting on a bend >45°, RCA stenting, and total stent length were the independent predictors for fracture of newer DES platforms, while closed-cell stent design (CS) was not.

Table 3
Comparisons of baseline characteristics between fracture subgroups in the newer DES platforms' group and Cypher Bx group.

Clinical characteristics (*n* = no. of patients)	Newer DES platformsFracture(+) (*n* = 18)	Cypher BxFracture(+) (*n* = 36)	*p*
Age, years	63.7 ± 10.5	67.9 ± 6.8	0.03
Male, *n* (%)	13 (72.2)	24 (67)	0.82
BMI (kg/m^2)	24.1 ± 2.8	24.3 ± 1.9	0.84
Index diagnosis, *n* (%)			
Stable angina	10 (55.5)	20 (55.5)	0.98
Unstable angina	4 (22.2)	9 (25)	0.85
AMI	3 (16.6)	7 (19.4)	0.86
Silent ischemia	2 (11.1)	0 (0)	0.23
Diagnosis at stent fracture detection, *n* (%)			
Stable angina	6 (33.3)	13 (36)	0.8
Unstable angina	2 (11.1)	2 (5.5)	0.73
AMI	0	0	
Asymptomatic	11 (61.1)	21 (58.3)	0.93
Diabetes mellitus, *n* (%)	5 (27.7)	11 (30.5)	0.93
Hypertension, *n* (%)	15 (83.3)	31 (86)	0.95
Current smoking, *n* (%)	6 (33.3)	9 (25)	0.5
Family history of CAD, *n* (%)	3 (16.6)	4 (11.1)	0.7
Previous MI, *n* (%)	5 (27.7)	4 (11.1)	0.16
Previous CABG, *n* (%)	1 (5.5)	0 (0)	0.97
LVEF (%)	61 ± 7	59 ± 14	0.76
Median duration from index PCI to detection of SF, months (IQR)	12.5 (9.2–15.5)	9.5 (6.3–13)	0.11

Angiographic characteristics (*n* = no. of lesion)	Newer DES platformsFracture(+) (*n* = 19)	Cypher BxFracture(+) (*n* = 36)	*p*
Target coronary artery, *n* (%)			0.45
LM	1 (5.2)	0	0.87
LAD	8 (42)	22 (61)	0.54
LCX	0	1 (2.7)	0.92
RCA	10 (52.6)	13 (36)	0.44
AHA/ACC type B2/C, *n* (%)	19 (100)	34 (94)	0.32
Reference diameter (mm)	3.18 ± 0.3	3.4 ± 0.3	0.03
Lesion length (mm)	45.5 ± 16.2	36.5 ± 9.9	0.03
Diameter stenosis (%)	79 ± 24	75 ± 10	0.28
Lesion angle >45°, *n* (%)	7 (36.8)	21 (58)	0.15
CTO, *n* (%)	3 (15.8)	1 (2.7)	0.13
Multivessel CAD, *n* (%)	15 (78.9)	22 (61)	0.66
Stent diameter (mm)	2.97 ± 0.32	3.18 ± 0.26	0.06
Maximum inflation pressure (atm)	14.3 ± 2.6	13.6 ± 2.5	0.4
Total stent length (mm)	48.3 ± 16.8	41.2 ± 10.9	0.09
Number of stents per lesion	1.58 ± 0.6	1.53 ± 0.7	0.77
Stent overlap, *n* (%)	11 (57.9)	19 (53)	0.6
Fracture type, *n* (%)			
Partial	9 (47.4)	9 (25)	0.15
Complete	10 (52.6)	27 (75)	0.28
Fracture site, *n* (%)			
Stent overlap area	10 (90.9)	20 (55.5)	0.06
Biggest angle at index CAG	12 (63)	31 (85)	0.12
Clinical outcome at follow-up, *n* (%)			
Binary restenosis	8 (42.1)	13 (36.1)	0.52
TLR	9 (47.3)	15 (41.6)	0.2

Values are expressed as mean ± SD or *n* (%) of patients except follow-up duration from index PCI to detection of stent fracture.
ACC, American College of Cardiology; AHA, American Heart Association; AMI, acute myocardial infarction; BMI, body mass index; CABG, coronary artery bypass graft; CAD, coronary artery disease; CAG, coronary angiography; CTO, chronic total occlusion; IQR, interquartile range; LAD, left descending artery; LCX, left circumflex artery; LM, left main coronary artery; LVEF, left ventricular ejection fraction; MI, myocardial infarction; RCA, right coronary artery; SF, stent fracture; TLR, target lesion revascularization.

DES fracture is an uncommon phenomenon. Little is known about the exact incidence of SF in the "real-world" patient population because it varies according to the type of population cohort, rate of follow-up angiography, definition of SF, and most of the earlier studies on SF focused on the initial platform of first-generation CBX. Clinically reported incidence of fracture of CBX ranged from 1.3% to 7.7% in previous observational studies [1–3], whereas data on fracture of the initial platform of first-generation paclitaxel-eluting stent (Taxus Express®) are rare. Nakazawa et al. reported a higher frequency (29%) of DES fracture in 177 post-mortem coronary lesions than those seen in previous clinical observational studies that utilized angiographic methods to detect SF [4]. This difference likely reflects the possibility that incidence of SF can be underestimated with imaging techniques used in clinical research compared with the methods for pathologic analysis of stents [5]. The newer platforms of DES have been upgraded compared with initial platforms of first-generation DES. The Cypher Select® stent is composed of a slotted tube, closed cell, 316L stainless steel, modified Bx Velocity™ stent with a longer undulating linker attached to the center of the stent struts resulting in improved flexibility, conformability and radial strength compared to the previous Bx Velocity™ stent which had a shorter linker attached to the end of stent crests. The Taxus® Liberté™ stent consists of a slotted tube, open-cell, 316L stainless steel, Liberté™ stent with 3 different stent designs according to stent diameter. It has thinner struts (0.0038 in.), smaller cell area, and more uniform strut apposition than the previous Express2™ stent, which may provide improved flexibility, vessel coverage, and support. The Endeavor® stent consists of a laser-welded modular design, open-cell, thin-strut (0.0036 in.), cobalt–chromium (MP35N), Driver® stent. The Xience™ V stent consists of a slotted tube, open-cell, thin-strut (0.0032 in.), cobalt–chromium (L605), Multi-Link Vision™ stent.

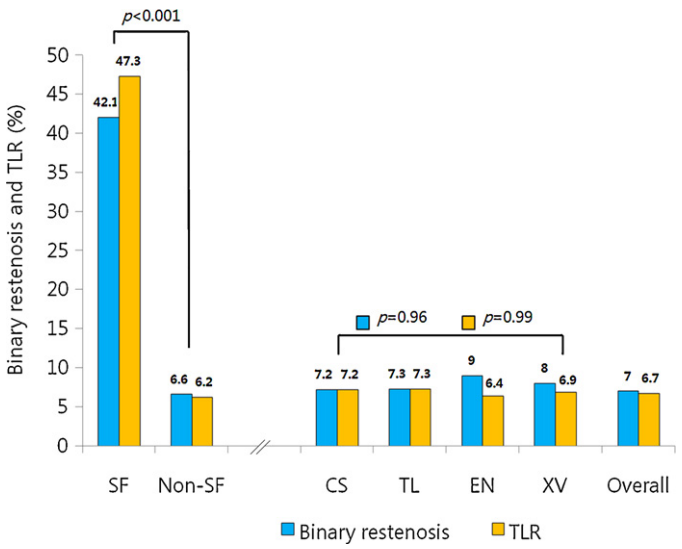

Fig. 2. Incidence of binary restenosis and target lesion revascularization (TLR) in the newer DES platforms. Although incidences of binary restenosis and TLR among the newer DES platforms were similar, those associated with stent fracture were significantly higher than those without it. SF, stent fracture subgroup; non-SF, non-stent fracture subgroup; TLR, target lesion revascularization. CS, Cypher Select®; TL, Taxus® Liberté™; EN, Endeavor®; XV, Xience™ V.

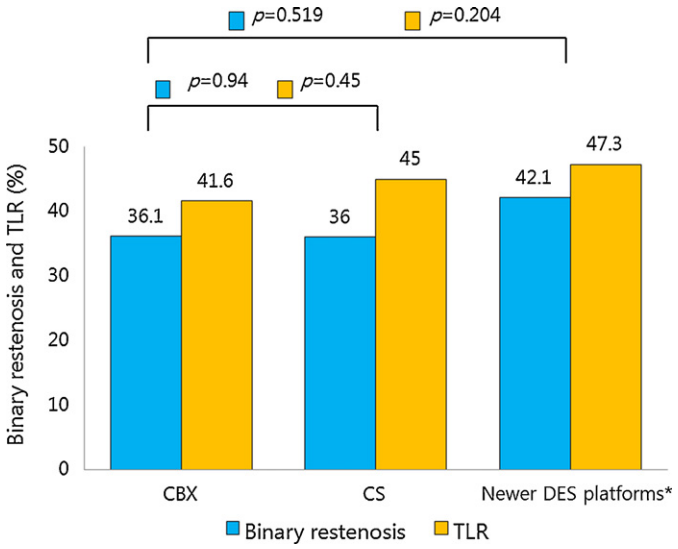

Fig. 3. Incidence of binary restenosis and target lesion revascularization (TLR) related with stent fracture in the Cypher Bx (CBX) group, the Cypher Select (CS) group and the entire newer drug-eluting stents (DES) platforms' group. Stent fracture-related binary restenosis and TLR of the CBX group were not different compared with those of the CS group and the entire newer DES platforms' group. *Including Cypher Select®.

These improvements in terms of mechanical and material properties of newer DES platforms may be a theoretical explanation of the significant low incidence of SF which was shown in the present study. Interestingly, no SF was found in patients implanted with the EN stent in our study. The EN stent has a cobalt–chromium alloy, thin-strut platform, and unique design (laser-welded modular design) which is different from that of other stents (slotted tube design). Recently, Enoki et al. provided the results of a fatigue test to compare the SF behavior using commercially available stents with different manufacturing methods (modular vs. slotted tube design) and materials (cobalt–chromium alloy vs. stainless steel) [6]. They reported that stents with modular structure demonstrated better behavior than slotted tube ones in the tensile-compression fatigue test, and stents made of cobalt alloy had a longer endurance due to its better mechanical properties than stainless steel. In addition, clinical reporting of EN stent fracture is rare; to the best of our knowledge, it has been reported in only 3 cases [7–9]. These lines of available evidence strongly support the results of our study. Although the SF incidence of newer DES platforms was statistically similar among stent types, the CS group showed numerically higher occurrence than the others. It is well known that closed-cell design stents are more rigid compared with open-cell design and this can cause more vessel straightening after implantation, which may make the stent more prone to fracture as the countervailing force of the vessel wall tends to revert the vessel axis to its original shape [10]. Furthermore, CS stent struts are more radio-opaque, making it easier to detect SF angiographically.

Patients with SF may remain asymptomatic or may present with an MI suggestive of stent thrombosis or recurrent angina suggestive of clinical restenosis [2,11,12]. In this study, a large portion of patients with SF were asymptomatic irrespective of stent type. The binary restenosis and TLR related with SF were much higher compared with those related with non-SF in both CBX group and newer DES platforms' group, which is in keeping with the findings of previous reports [2,3,13]. Moreover, it is notable that SF-related binary restenosis and TLR rates of the newer DES platforms' group were similar to those of the CBX group. These findings may imply that clinical outcomes of SF remain not so favorable despite use of newer DES platforms which may lower the incidence of SF. The angiographic pattern of restenosis in all patients with SF was focal,

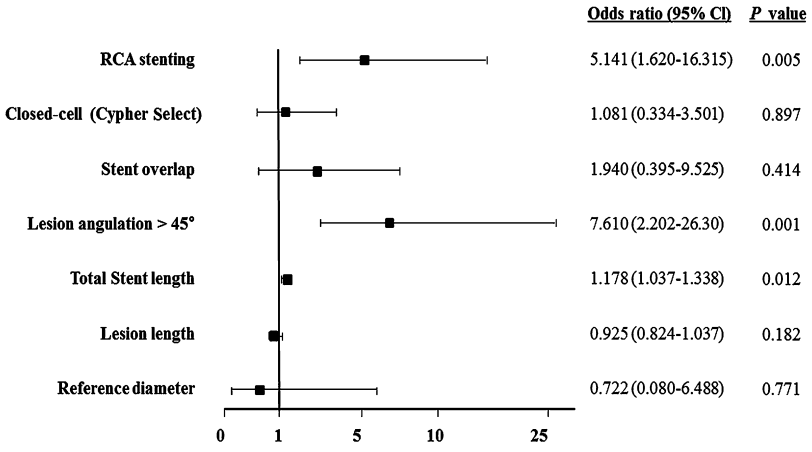

Fig. 4. Independent predictors of fracture in the newer DES platforms. RCA, right coronary artery.

which is consistent with the findings of several previous studies [1,3,13]. For the mechanism showing how focal restenosis is related to SF, it has been suggested that lower drug delivery at the fracture site may not be effective in suppressing neointimal hyperplasia and an increase in local mechanical irritation by the fractured struts can cause smooth muscle proliferation and inhibit re-endothelialization, resulting in focal in-stent restenosis [13,14].

Features that have been associated with susceptibility to SF in previous studies include long stent, RCA stenting, stent design (closed-cell design), overlapping stent, and excessive vessel angulation [1,3,15,16]. Consistent with these reports, total stent length, lesion angulation >45°, and RCA stenting were significant predictors for fracture of newer DES platforms in the present study. Similar to the observations in several reports [3,14,15], all SFs of newer DES platforms occurred in long stented lesions, i.e. ≥28 mm, with a mean stent length of 48.3 mm. Longer stents compared with shorter ones can be more prone to fracture owing to higher radial forces [14]. Additionally, SF is relatively common at the "hinge" point where the mechanical stress to stent strut is greatest. The overlapped stent edge and an excessive angle (lesion angulation >45°) on the initial CAG can work as hinges [17]. Out of 19 fractures of newer DES platforms, 15 SFs were located at the hinge point which was adjacent to the edge of overlapped stent (10 cases) or the biggest angle (12 cases) on initial CAG. In the present study, however, overlapping stent did not show statistically significant association with the occurrence of fracture using multivariable regression analysis after adjusting for several confounders, while it showed statistically significant association with stent fracture using univariable regression analysis (unadjusted HR: 7.936; 95% CI: 3.07–20.5; $p < 0.001$). Finally, the RCA usually has greater curvature and more vessel movement during the cardiac cycle than the LAD and LCX providing specific conditions that are more prone to SF. Considering findings of the present study, it is clear that precise evaluation of lesion characteristics remains very important to predict SF, even in the era of newer DES platforms.

This study has several limitations that merit mention. First, the fluoroscopic and angiographic methods which were used to diagnose SF in our study, have a limited resolution power to detect SF compared with new technology such as the Stentboost (Philips Healthcare, Best, Netherlands), which can show enhanced stent strut shadows, and intravascular ultrasound was not mandatory. Thus, our study may have underestimated the frequency of SF. However, we tried to overcome this resolution limitation using additional detection methods such as increased magnification, image without contrast and image with inverted color. Second, the definition of newer DES platforms may seem arbitrary. In general, all platforms of Cypher and Taxus stents are considered as a same first-generation DES. However, although platforms of Cypher Select® and Taxus® Liberté™ were improved from the initial ones, little was known about clinical data on SF of these newer platforms. Thus, we sought to evaluate the impact of the newer DES platforms which have been used widely in current practice on SF and therefore, Cypher Select® and Taxus® Liberté™ were categorized into the newer DES platforms' group. As a result, we could observe a significant difference in the SF incidence between the CBX group and the newer DES platforms' group. Third, among newer DES platforms, enrolled lesion numbers of the EN group were relatively small. This may act as an unintended bias to evaluate true incidence of SF of EN. Fourth, the study design was a retrospective analysis; therefore, it is subject to the limitations inherent to all such analyses.

In conclusion, this study shows that implantation of newer DES platforms might reduce incidence of SF compared with CBX. However, when SF occurs, the rates of binary restenosis and TLR remain similarly high. Lesion characteristics on index PCI are more important than the type of implanted stent to predict SF in the newer DES platforms' era.

Conflicts of interest

None declared.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jjcc.2012.07.011.

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